

In the United States Patent and Trademark Office

Applicants: Matthieu Guitton *et al.*

Serial No.: 10/812,298

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For: **METHODS FOR THE TREATMENT
OF TINNITUS INDUCED BY COCHLEAR
EXCITOTOXICITY**

Confirmation No.: 1803

Examiner: Jennifer Kim

Art Unit: 1617

Attorney Docket No.: 067802-3000-001

SUPPLEMENTAL DECLARATION UNDER 37 CFR §1.132

Dear Sir:

I, Richard J. Salvi, Ph.D., declare and state as follows:

1. I am employed as Professor, University at Buffalo; Dept. Communicative Disorders and Sciences 1987-present; Clinical Professor of Otolaryngology, University at Buffalo, Dept. of Otolaryngology; Clinical Assistant Professor, University at Buffalo, Dept. of Neurology, 1997-present; Clinical Professor, Univ. of Rochester, Dept. of Otolaryngology, 1997-present;

- I received my Ph.D. in Experimental Psychology from Syracuse University in 1975.
- I received my B.S. in Psychology from North Dakota State University in 1968.

2. I submitted a declaration under 37 C.F.R. § 1.132 in the above-referenced U.S. patent application (the '298 application) on January 7, 2010 (the "Declaration").

3. The statements I made in the Declaration apply with equal weight, force and effect with respect to the invention as claimed in the claims pending in the '298 application as of December 29, 2008 (Exhibit A); as submitted (but not entered) September 30, 2009 (Exhibit B) and as submitted on January 7, 2010 (Exhibit C).

40. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States

Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Richard J. Salvi, Ph.D.

2/16/2010

Date

Exhibit A – Claims submitted December 29, 2008

1. A method for treating tinnitus induced by cochlear excitotoxicity in a human, the method comprising administering to a human a therapeutically effective amount of a pharmaceutical composition comprising the NMDA receptor antagonist ketamine, effective to suppress or reduce NMDA receptor mediated aberrant activity of the auditory nerve in a human in need of such treatment and correlating the administration of ketamine with a reduction in tinnitus and with suppressed or reduced NMDA receptor-mediated aberrant activity of the auditory nerve.
2. (Canceled).
3. (Canceled).
4. The method of claim 1 wherein the cochlear excitotoxicity is provoked by an occurrence selected from the group consisting of acoustic trauma, presbycusis, ischemia, anoxia, and sudden deafness.
5. The method of claim 1 wherein the pharmaceutical composition is administered topically/locally via the round window membrane or the oval window membrane to the inner ear.
6. The method of claim 1 wherein the pharmaceutical composition is administered topically/locally by means of invasive drug delivery techniques to the inner ear.
7. The method of claim 4 wherein the cochlear excitotoxicity is characterized as acute.
8. The method of claim 4 wherein the cochlear excitotoxicity is characterized as repeated.
9. The method of claim 4 wherein the cochlear excitotoxicity is characterized as prolonged or chronic.

Exhibit B – Claims submitted (but not entered) on September 30, 2009

1. A method for treating tinnitus induced by cochlear excitotoxicity in a human, the method comprising administering to the human a therapeutically effective amount of a pharmaceutical composition comprising the NMDA receptor antagonist ketamine, effective to suppress or reduce NMDA receptor mediated aberrant activity of the auditory nerve in the human in need of such treatment and correlating the administration of ketamine with a reduction in tinnitus.
2. (Canceled).
3. (Canceled).
4. The method of claim 1 wherein the cochlear excitotoxicity is provoked by an occurrence selected from the group consisting of acoustic trauma, presbycusis, ischemia, anoxia, and sudden deafness.
5. The method of claim 1 wherein the pharmaceutical composition is administered topically/locally via the round window membrane or the oval window membrane to the inner ear.
6. The method of claim 1 wherein the pharmaceutical composition is administered topically/locally by means of invasive drug delivery techniques to the inner ear.
7. The method of claim 4 wherein the cochlear excitotoxicity is characterized as acute.
8. The method of claim 4 wherein the cochlear excitotoxicity is characterized as repeated.
9. The method of claim 4 wherein the cochlear excitotoxicity is characterized as prolonged or chronic.

Exhibit C— Claims submitted January 7, 2010

1. A method for treating tinnitus induced by cochlear excitotoxicity in a human, the method comprising administering to the human a therapeutically effective amount of a pharmaceutical composition comprising the NMDA receptor antagonist ketamine, effective to suppress or reduce NMDA receptor mediated aberrant activity of the auditory nerve in the human in need of such treatment and correlating the administration of ketamine with a reduction in tinnitus and with suppressed or reduced NMDA receptor-mediated aberrant activity of the auditory nerve.
2. (Canceled)
3. (Canceled)
4. The method of claim 1 wherein the cochlear excitotoxicity is provoked by an occurrence selected from the group consisting of acoustic trauma, presbycusis, ischemia, anoxia, and sudden deafness.
5. The method of claim 1 wherein the pharmaceutical composition is administered topically/locally via the round window membrane or the oval window membrane to the inner ear.
6. The method of claim 1 wherein the pharmaceutical composition is administered topically/locally to the inner ear.
7. The method of claim 4 wherein the cochlear excitotoxicity is acute.
8. The method of claim 4 wherein the cochlear excitotoxicity is repeated.
9. The method of claim 4 wherein the cochlear excitotoxicity is prolonged or chronic.
10. A method for treating tinnitus induced by cochlear excitotoxicity in a human, comprising administering to the human a therapeutically effective amount of a pharmaceutical composition comprising ketamine.
11. The method of claim 10, wherein the normal auditory neurotransmission is not affected.
12. The method of claim 10, wherein the pharmacological composition comprises a ketamine analog, a ketamine derivative or a ketamine enantiomer.
13. The method of claim 10, wherein the ketamine is (S)-ketamine.
14. The method of claim 10, wherein the ketamine is enantiomerically enriched for (S)-ketamine.